



*A case of leprosy, with remarks on the nature of the lesions
found in the lungs.*

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I. PRELIMINARY REMARKS.

THE case forming the subject of this communication came under the care of Dr. Cavafy at St. George's Hospital in August, 1888. While the patient was in the wards we examined on

several occasions many of his cutaneous lesions for the purpose of discovering bacilli, and if possible of cultivating these organisms. On the death of the patient one of us had opportunity to remove portions of various organs. Dr. Cavafy, knowing that we had taken some interest in the case, very kindly gave us permission to make what use we thought fit of the material thus obtained, and also of the notes which had been collected whilst the patient was under treatment. In this paper we do not wish to give an exhaustive account of all our observations, or to repeat what has already been well described in former cases, as this would render the communication unwieldy. We therefore confine ourselves here to a general survey of the lesions, of the distribution of the bacilli in the various organs, and especially to a consideration of the pulmonary lesions. For some time before his death the patient had suffered from symptoms similar to those of rapidly advancing phthisis, and the question arose whether this was due to an extension of the leprous process to the lungs or to a superadded tuberculosis; a question we did not feel able to resolve by an examination of the sputa. This question was naturally pursued in the examination of the *post-mortem* material.

II. HISTORY OF THE CASE.

The following is a short *résumé* of the case, based on the patient's statements and the notes taken in hospital.

J. R—, aged 24, admitted into St. George's Hospital on August 25th, 1888. He was born in India, on the Coromandel Coast, of English parents. His family seems to have been free from tubercular taint. When still a baby he was taken to St. Thomas's Mount, in Madras Presidency, and remained there until he was seven years old, when he went to England.

Nine years later, when aged sixteen, he returned to India, and was quartered at Bellary, in Madras. Lepers are said to be common there.

Five months after his return he noticed swellings in both cheeks, which remained for six weeks and then disappeared. Swellings then appeared on the front of both thighs, which were painful and prevented walking. During this period, which dates from March, 1880, he suffered from continued fever, and was in hospital from March to August of that year.

He then spent two years in the hills, during which time no fresh swellings appeared, while the sites of the old ones became pigmented.

He was then sent back to Bellary, and again suffered from continued fever for three months.

In 1884—four years after the first outbreak—swellings appeared on the back and legs.

In 1885 the voice was noticed as altered.

In 1886 the first phalangeal joints enlarged, and he was in hospital for laryngeal catarrh. During this time “lumps” developed rapidly—sometimes in a few hours; and the diagnosis of leprosy was, according to the patient, first made.

In 1887 he was discharged, and there was very little change in his condition until shortly before his admission, when he began to suffer from cough and night sweats.

On his admission in August, 1888, he had a typical leonine aspect, with hairless face, thickened subcutaneous tissue of brow, nose, and cheeks, and large and pendulous ears. The nasal bridge was also depressed. The skin was smooth and of a sallow colour. The trunk was covered with discrete tubercles, both superficial and deep. There was a scab on the right elbow, and a scaly patch over the left, while numerous tubercles and maculæ were situated on the extensor surfaces of the upper arms. The skin over the back of wrists and hands was thickened, reddened, and scaly. The first phalanges were enlarged, and the nails convex and split longitudinally in the middle line. There were also tubercles on the thighs, together with scars of an old ulcer on each ham. Over the ankles and lower part of the legs there were several small ulcers with raised edges, covered with feeble granulations which exuded a moderate amount of pus.

Two or three small anæsthetic patches were noted on the anterior surfaces of the arms.

At the time of his admission the signs of pulmonary disease were extremely slight.

During September and October, 1888, several attempts were made by us, independently and together, to cultivate the *Bacillus lepræ*.

The patient improved somewhat in hospital until he left in the winter of 1888. He then seems to have suffered severely from privation and cold, and, after a short time at St. Thomas's Hospital,

returned on May 29th, 1889, to St. George's Hospital, suffering from extensive lung disease. After some time a pneumothorax developed, and the patient died on July 13th.

During the second period of the patient's stay in the hospital the sputum was examined on many occasions by both of us, and always found to contain bacilli.

These bacilli varied considerably in number. At times they were extremely abundant, and often formed clumps of a size seldom seen in ordinary tuberculosis. It was also common to find them grouped in small epithelial-looking cells—an appearance which, though met with occasionally in tuberculosis, is by no means frequent.

III. POST-MORTEM EXAMINATION.

The body was very thin, and had an offensive smell differing from that of simple putrefaction.

A. *Skin: macroscopic appearances.*

The skin was generally, but unevenly, darker than normal, dirty and rough-looking. The hair was very thin all over the body and almost entirely absent from the face, there being no eyebrows, eyelashes, or hair on the lips and chin.

The *face* presented, in typical form, the usual appearances associated with tubercular leprosy. The ears were much deformed and nodulated, and the lobule enlarged and pendulous. The border of the right helix was ulcerated for about one inch of its extent. The bridge of the nose was depressed.

On the *trunk* there were numerous maculæ and tubercles, and some leucodermic patches. The most marked maculæ were in the left hypochondriac region; and while some of them were uniformly brown all over, others had become white in the centre and had a thin pigmented zone at their margin. Many of these maculæ were evidently over very flat and indistinct tubercles, while others were apparently true maculæ. The white centre of some of the pigmented patches was distinctly depressed.

On the *limbs* the skin was pigmented, dry, scaly, uneven, and dirty-looking as elsewhere, but in addition presented numerous destructive lesions in the shape of ulcers and fissures. Amongst

the most noticeable was a small ulcer on one of the knuckles of the left little finger, and fissures at the level of the phalangeal articulations. There was also a marked shrivelled leucodermic patch, surrounded by a zone of pigmentation, over the second phalanx of the left little finger.

There were pigmented scars about the legs and ankles, and among these were two very evident ones about 2 inches in diameter over the shin of each leg. There were also four smaller ulcers over the right trochanter, which seemed to correspond each to a single tubercle whose central part had become necrosed. The largest of these ulcers was oval, and measured about $\frac{3}{4}$ inch in diameter, the others being smaller. Owing to their occurring in the centre of a nodule their edge was raised, but it was not clear whether there was any true inflammatory thickening. These ulcers had a very regular round or oval shape, with a very abrupt border and a bottom comparatively smooth, and occupied by a layer of granular *débris*. The skin around was distinctly pigmented.

Several specimens of skin were taken for microscopical examination. They were selected for the purpose of following the various steps of the processes leading to the lesions just described, and included—

1. Skin of the back of the wrist, slightly pigmented, dry, and scaly-looking, with small granular swellings, difficult to see but easy to feel, and not presenting typical leprous tubercles or very marked thickening.

2. Skin of abdomen with a leucodermic patch in the centre of a very slightly raised pigmented patch (macula?).

3. Skin of ulnar side of last phalangeal joint of left little finger with a fissure.

4. Skin over first phalangeal joint of little finger with a very small ulcer which had begun in a fissure, and was covered with a scab.

5. Ulcer of ear, which was apparently spreading. (This is the only ulcer examined in whose discharge bacilli were at all abundant.)

6. Ulcerated tubercles over the great trochanter.

It will be evident from this list of lesions that the various parts of the skin were most unequally affected. The most marked lesions were observed in the head, arms, and legs. The skin of the trunk was less affected than that of the extremities, and the proximal segments of these less than the distal,

Microscopic examination.—The slightly nodulated skin of the back of the wrist can be taken as a type, to which the skin of the other parts of the body may be compared.

The *epidermis* is uneven in thickness, being generally thinner over the slight nodules, and thicker in the intervening shallow furrows. Some of the cells of the rete Malpighii are swollen or even vacuolated, and there is, generally speaking, an increase of pigmentation of the deep cells. This increase is most conspicuous sometimes at the sides, sometimes over the centres of the nodules. The opening of the sweat-glands is generally obliterated.

The *cutis vera* is considerably altered. The superficial papillæ are flattened, especially over the nodules, while the whole membrane presents an unusually homogeneous appearance. It is uneven in thickness, and presents at intervals nodular projections which correspond with those felt by the finger during life. All through the corium, but especially in the midst of the swellings, a large number of angular bodies are found; some of these are evidently cells with nuclei, others are of doubtful nature. These cells form flattened fusiform tracts between bundles of fibrous tissue, and look like small epithelioid cells. Under a high power they have a granular appearance, are very translucent, and seem swollen. With logwood and eosin they stain faintly, sometimes staining more with one and sometimes with the other of these dyes. Many are vacuolated, and have at least one comparatively large rounded clear space in their centre. Among these small cell-groups, other large, generally oval, though sometimes round and almost cylindrical bodies can be seen. Most of these large oval bodies (leprous cells) are vacuolated, while many have a very large central vacuole, looking much like the lumen of a duct or vessel. This is itself surrounded by a thick granular wall, in which smaller rounded vacuoles are found. These bodies stain faintly with logwood and eosin, and are stained pink with picro-carmin. After the action of this last stain they are seen to contain bundles of short fibrils, which have sometimes a very definite arrangement. At the periphery of such masses there is sometimes a group of nuclei, but generally the oval masses are separated from the walls of the cavities containing them by a clear space, and seem to be quite loose in that cavity. In the deeper layers of the skin these masses, large and small, seem often to be grouped round the atrophied sweat-glands. This almost complete atrophy of the sweat-glands gives

to the deep layers of the skin a peculiar homogeneous appearance. Here and there long angular spaces are found, filled with degenerated cells and fatty granules. These spaces are surrounded by fibrous walls, and seem to have been vessels.

The *fatty subcutaneous tissue* is affected much in the same way but less than the cutis.

After staining such sections with carbolised or anilised fuchsin for from 15 minutes to 24 hours, and decolourising with sulphuric or nitric acid, a prodigious number of bacilli having all the characters of those of leprosy are brought out. These bacilli are most abundant in the cutis vera, and especially in the deeper parts of that structure. They are also pretty abundant in the subcutaneous tissue among the fat lobules. They are found as usual either free between cells, or in the epithelioid cells described as forming long tracts, or in the large vacuolated cells or masses which are the so-called leprosy cells. They also form small clumps in the superficial portions of the cutis. Some of the small masses are spindle-shaped, like ordinary fixed connective-tissue corpuscles, while others are round but generally smaller than leucocytes. Large masses of these bacilli are also found in the large degenerated tracts which are seen in the deeper parts of the skin in some places.

These bacilli differ much in appearance. The free ones and those which are contained in small cells are, generally speaking, short and straight, and stain readily, but are comparatively easy to decolourise. They are very distinct, owing to the parts surrounding them being easily decolourised or taking well the counter-stain. In the leprosy cells the bacilli are longer, more beaded, and grouped in fasciculi which have often a very distinct arrangement in relation to the vacuoles. The substance separating these bacilli is difficult to decolourise, and the bacilli themselves seem to stain of a deeper colour than the short discrete ones, and they are also much more difficult to decolourise.

Many of these large leprosy cells evidently occupy the lumen of lymphatic vessels which they distend, but some undoubtedly originate in the midst of the tracts of smaller epithelioid cells, some of which, either by coalescence or by growth of the bacilli, gradually become larger. Even in the lymphatic vessels the bacilli seem at the beginning to grow in the endothelial cells. The nucleus of cells in which numerous bacilli are found stains badly or not at all, and appears in many cases as a vacuole on the surface of which the

bacilli are grouped. When the bacilli are very few it is, however, sometimes possible to see them in one part of the protoplasma of a cell which is still distinctly nucleated. In some cases such a cell has several nuclei at the periphery of a large mass of vacuolated protoplasma, in which a few groups of bacilli are visible also. These cells are really giant-cells.

A few small groups of bacilli or individual bacilli are found in the walls of blood-vessels, chiefly in those of the veins and capillaries; they can be seen distinctly to grow on the endothelial lining. As has been previously noticed, the cuticle seems to be almost always free from bacilli, even over those parts where these come quite near to the deepest layers of the rete Malpighii. There are, however, a few exceptions to this rule.

The skin of the wrist, which has just been described, contained a number of tubercles which, for leprosy, were small, being scarcely larger than ordinary tubercles. It was in these tubercles that the leprous cells were the most abundant.

The skin of the abdomen, in the region of a leucodermic patch with a pigmented somewhat raised border, showed very similar but less extensive lesions. The epidermis corresponding to the depressed pale centre was very thin and contained but little pigment, while the border of the patch was thicker and deeply pigmented.

The pigment was situated in the deep cells of the rete Malpighii, and had all the appearances of melanin.

The true skin is less altered here than in the last part described, but is a little thicker than normal. The sweat-glands are less altered than in the other regions examined, but are generally surrounded by tracts of small cells containing many bacilli. Many of these are also in leprous cells. The leprous cells are less abundant in this region than on the back of the wrist.

Skin with a fissure (little finger).—The fissure after section is found not to extend deeper than the horny layer of the epidermis, which is thickened and lamellated in that region. Immediately under that fissure there is a large mass of leprous cells and of bacilli, free or in epithelioid cells. The bacilli come in contact with the epithelial cells of the rete Malpighii, but do not seem to penetrate into them. The papillæ are flattened in that region, but on both sides and at a very short distance from the fissure the papillæ are large again, and the rete Malpighii hypertrophied and much pigmented.

*Skin with a small ulcer covered with a scab (little finger).—*The cuticle is destroyed over a very narrow area; on both sides of the small fissure-like ulcer the epidermis is thickened and pigmented. The bottom of the ulcer is formed by a little granulation tissue, covered with very little granular *débris* and a scab. Bacilli are extremely abundant both under the ulcer and around it; but although they come quite near the epidermis in the neighbourhood of the lesion, yet *no free bacilli are found in the granulation tissues nor in the scab*. A few leprous cells are near the bottom of the ulcer, but are certainly small and very few compared with those found in the adjacent corresponding parts. *No leprous cell is found among the products accumulated on the surface of the small wound*. The subcutaneous tissue, tendons, and periosteum, as well as the bones covered by the skin just described, all contain a large number of bacilli. The cutis is much congested, and the walls of the distended capillaries are literally covered with the parasite. The walls of the veins contain groups of bacilli, and some of these are even seen in the endothelium lining the lumen of the vessel. Some arteries have their intima thickened, and have also bacilli in the other layers of their wall.

The skin of the ear shows very much the same lesions, but much exaggerated in intensity. The accumulation of bacilli, both discrete and in leprous cells, is extraordinary; and these bacilli, both free and in cells, are also pretty abundant in the granulation tissue forming, and in the pus or exudation covering the bottom of the ulcer. A few bacilli are also found penetrating into the epithelial sheath of hair follicles and the outer strata of sebaceous glands. This has also been noted previously by Babes.

The skin over the trochanter with rounded excavated ulcers, apparently following necrotic softening of tubercles. The epidermis covering the border of these ulcers overlapped slightly the edge of the lesion, and the bottom of the ulcer was covered with granular *débris*, among which were a few masses of micrococci, but no *Bacillus lepræ*. The bacilli were, however, pretty abundant not far below the surface, and distributed in the usual way in the true skin and subcutaneous tissue. Some of the arteries were almost entirely obliterated by endoarteritis, and had in their walls many bacilli; these were, as in other places, most abundant in the perivascular lymphatics. Many of the veins of that region were filled with coagulated blood, or simply a network of fibrin.

B. *Bones, articulations, &c.*

The two most noticeable features at the autopsy were the depression of the ridge of the nose, and the looseness of the phalangeal joints.

The only bones and joints taken for *microscopical investigation* were those of the fingers.

In a section including a phalangeal joint it is found that there is distinct osteomyelitis, leading to the enlargement of a number of Haversian spaces, and to the accumulation within them of very vascular cellular tissue, in the midst of which are numerous large fat-cells, and large oval and round vacuolated cells, which look like other leprous cells, except that the bacilli which they contain are more granular-looking, and less densely packed than in ordinary leprous cells. The bacilli are found extending as far as the cartilage, but do not penetrate into that tissue.

The *periosteum*, the *fibro intra-articular disc*, the *ligaments*, all contain bacilli, but neither the cavity of the joint itself nor the articular cartilages contain any bacilli. The tendons of the long flexors and extensors also contain a few, but very few, small groups of bacilli, which seem to be in tendon corpuscles.

c. *Pharynx, larynx, and trachea : macroscopic examination.*

The mucous membrane of the pharynx and larynx was much affected, and the lesions found in that membrane were very similar to those found in the skin.

The epiglottis was unevenly thickened, irregular in outline, and thick. Its mucous membrane was rough, and presented superficial erosions or ulcers, especially on its posterior aspect, and below the cushion. Here the ulceration extended between the anterior extremity of the vocal cord, in the region of the central fossa, down into the larynx. The false and true vocal cords were also much thickened, as well as the mucous membrane covering the arytaenoid cartilages. All these parts had a rough, or granular, somewhat eroded look, with the exception of the true vocal cords, which had retained part of their natural smoothness.

The mucous membrane of the lower part of the larynx and of the trachea was irregularly thickened, and showed numerous shallow ulcerations or erosions.

Microscopically, the epithelium is found shed from the surface of the mucous membrane almost everywhere, except at the level of the true vocal cords. Below the vocal cords these superficial layers of the mucosa are infiltrated with small cells and partly necrosed. The mucous glands are much altered. Their epithelial cells are generally in a state of disintegration, except those of the ducts, which have in many places multiplied and are very clear. The mucous and submucous layers are infiltrated with groups of epithelioid cells like the corresponding part of the skin; but these small cells are, generally speaking, less numerous; whilst large multinucleated masses of protoplasm resembling closely giant-cells, but much vacuolated, are, on the contrary, more abundant than in the skin.

The thyro-arytænoideus muscle is in a state of interstitial myositis, with considerable atrophy of some of its fibres. Some of the small nerves are in a corresponding state of interstitial inflammation.

Bacilli are extremely abundant just beneath the surface of the true vocal cord, where they are found both discrete and in leprous cells. They are less abundant above and below the cord, where the mucous membrane is denuded. A few bacilli penetrate into the epithelial strata, but whether they are in epithelial cells or between them is extremely difficult to ascertain. Some seem to be in small wandering corpuscles; but as nuclei are extremely seldom evident in the small rounded masses to which we allude, it is difficult to affirm that they are actually what we suppose them to be. A few bacilli are undoubtedly free in the ducts of some mucous glands. A few bacilli, isolated or in clumps, are also found among the granular products covering the ulcerated membrane of the larynx. The great bulk of the bacilli is, however, found, as in the skin, at some distance from the surface, and apparently in the lymphatics surrounding blood-vessels, glands, and nerves, and also in the connective-tissue corpuscles or lymphatic spaces of ordinary fibrous connective tissue.

The laryngeal muscles are also invaded by the parasite, which is mostly located in large cells situated in the endomysium separating the muscular fibres; in some instances, however, the bacilli have passed through the sarcolemma, and seem to form colonies, either in the muscle corpuscles or between the sarcolemma and the muscular fibre, which in such cases is much altered. These bacilli are very short and thick, many almost oval and worm-

like; they, however, give the typical reaction of the *Bacilli lepræ*. The bacilli found in the larynx are, generally speaking, very short and thick.

D. *Lungs and pleuræ.*

Pleuræ.—There were dense fibrous adhesions over the greater part of the upper lobe of the left and of the right lungs. These adhesions were more extensive on the left than on the right side. Both pleuræ, but more specially the left, contained an excess of serous fluid. The visceral layer was, generally speaking, thickened, more opaque, less even and shiny than normal, even in those parts where there were no adhesions.

Lungs.—They weighed together 4 lbs. The right one was heavy, and did not collapse on the pleura being opened. The lower lobe of the left one had retained part of its elasticity. The right lung was in a general state of intense congestion and induration; the lower lobe was oedematous. All through the organ there were small, pale, creamy yellow patches, some hardly larger than a millet seed, but many, especially near the apices of the upper and lower lobes, very much larger. These cheesy-looking patches had often a distinct arborescent arrangement, and seemed to be occupying the lumen of small or large bronchi. At the upper part of the lower lobe, and also at the apex of the right lung, there were cavities filled with soft caseiform products which communicated with bronchi. One of these cavities was almost cylindrical, measuring over $1\frac{1}{2}$ inches, and seemed to be a bronchus with degenerated walls.

The upper lobe of the left lung was almost entirely replaced by a large cavity full of curdy-looking blood-stained fluid, containing a large number of small cheesy-looking masses. This cavity was surrounded by dense fibroid lung tissue, undistinguishable in some places from the thickened pleura. Septa of the same nature subdivided the large cavity into compartments. Both the walls and septa were covered with thick cheesy-looking matter, and contained in their depth cheesy-looking nodules. The walls were also deeply congested.

The lower part of the upper lobe, which was not entirely destroyed, was consolidated, and contained a very large number of large cheesy nodules.

The lower lobe was beset with pretty large cheesy-looking tubercles or broncho-pneumonic patches, between which the parenchyma was congested and indurated.

There was no evidence, either in the right or in the left lung or pleura, of anything resembling a miliary tubercle. The general characters were those of a very extensive cheesy broncho-pneumonia, such as is observed in cases of tuberculosis of the lungs beginning in the bronchi or peribronchial tissues.

This impression was entirely confirmed by *the microscopical examination*. The least affected bronchi were in a state of acute inflammation, with shedding of their columnar epithelium and filling up of their lumen with purulent-looking exudation, the epithelial cells being shed so rapidly as to form in rare cases continuous masses in the midst of the small-cell exudation which distends their lumen. The mucosa and adventitious coats of such bronchi are infiltrated also, and contain a large number of epithelioid cells. The neighbouring alveoli are also distended, sometimes with almost nothing but large epithelioid cells, very transparent and vesicular-looking, sometimes by blood or coagulated lymph more or less altered.

In somewhat more diseased bronchi the walls are still visible, as well as some degenerated tracts of epithelial cells; but the lumen, which is now irregular and not very distinct, is occupied mainly by breaking-down cells and fatty *débris*. The infiltrated alveoli are numerous, and their contents either undergo the same changes as those of the bronchi, or else the congested alveolar walls become thicker, owing to the accumulation of cells and congestion of their vessels. The epithelioid cells occupying the alveoli form continuous epithelial-looking masses without undergoing degeneration. In such regions the appearance is not unlike that of an adenomatous mass. The cells, although staining pretty well, have a distinct tendency to coalesce. In none of the lesions described so far is it generally possible to discover any bacillus staining like that of tuberculosis or leprosy. Small clumps of cocci, staining badly with methylene blue and sometimes with hæmatoxylin as also some slender bacilli staining with methylene blue, were thought to be present in some of the bronchi, but this did not seem to be the rule.

Larger tracts of degenerated cellular products, having relations to surrounding parts similar to those just described as connected with bronchi, correspond to the larger cheesy masses which were so distinct at the *post-mortem* examination. In the midst of such patches it is often possible to distinguish some remains of a canal

surrounded by more or less distinct meshes, and these appearances doubtless indicate the previous existence of a bronchus and of the alveoli surrounding it. At the periphery of such masses there is usually a zone of badly formed granulation tissue, and in or outside that zone most of the alveoli are distended with epithelioid cells, many of which seem to have coalesced to form giant-cells, which in some cases are of prodigious size. A few smaller giant-cells are undoubtedly formed in lymphatic vessels, and look more like those generally observed in miliary tubercles. As a rule, however, the giant-cells are not surrounded by any fibrous tissue, dense or loose, but either lie distinctly in a cavity or are surrounded by more or less distinct epithelioid cells, distending some cavity which in many cases is clearly an alveolus. Nearly all these giant-cells contain a large amount of carbon particles: a few appear to contain some bacilli, staining blue.

All the parts surrounding these large cheesy patches are intensely congested, the vessels looking at least as large and as numerous as in advanced cardiac congestion. In many places this is accompanied by hæmorrhages or by exudation of coagulable lymph into the few alveoli which are not yet filled up. It is in the centre of these large cheesy patches that bacilli can be found abundantly, and sometimes form large bushy masses (*bacilles en broussaille*).

These bacilli are extremely variable in characters. In some places they are short and thick, straight or curved, and in other places long, slender, and beaded, or not. They, however, in the most advanced lesions have most unmistakably the same staining reactions as the *Bacillus lepræ* found in the most typical lesions of the skin and other organs. In addition to these, however, there are often associated organisms, staining more or less distinctly with methylene blue, sometimes coccoid, sometimes bacillary in character.

Bacilli giving the typical reaction with fuchsin are generally found abundantly in the centre of the lesions. There is often a distinct zone of blue organisms in the region intermediate between the central colony and the granulation tissue limiting the lesion. We merely mention the fact as being of possible importance, but do not wish to discuss it more fully here.

When these masses have reached the size of a large pea they begin to soften in the centre, and when this happens, the red bacilli become so abundant as to form an almost pure cultivation,

if it were not for the presence of the blue cocci and bacilli to which we have just alluded, and of which a few clumps are found here and there. The cheesy-looking material, which has been described as covering the walls of the large cavity in the left lung and forming the small masses floating in the blood-stained fluid, was found immediately after the *post-mortem* to be, practically speaking, composed of nothing but bacilli, staining extremely readily, and resisting decolorisation as well as the bacilli found in the skin.

The other lesions found in both lungs were connected with the pleura and interstitial tissue.

The serous and the subserous layers of the pleura were considerably thickened nearly all over the left lung, much less so on the right side.

The serous layer was also in part covered with a fibrous exudation. The thickening is mainly due to the formation of a very hyaline, rather cellular, and very vascular fibrous tissue. Giant-cells are pretty abundant in the pleura, and seem to be in the lymphatic vessels, as all transitions can be seen between long tracts of nuclei, in a cylindrical homogeneous mass occupying the position of a lymphatic vessel, between parallel blood-vessels, and the usual form of giant-cells. None of these giant-cells seem to form the centre, or to enter into the formation of any neoplastic-looking lesion; and the tissues immediately surrounding them do not differ from those wherein giant-cells are found.

In the subserous layer of the pleura swollen epithelioid cells are found, and sometimes lymphatics with ordinary lymph-corpuscles.

On the surface of the serous layer, bacilli, free, or in a few cases distinctly enclosed in small epithelioid cells, are found in moderate amount; most of these are short and thick, but some are long and slender.

The interlobular and interalveolar septa, when they are not involved in the lesions already described, are intensely congested and infiltrated with epithelioid cells, so that they are often undistinguishable from the contents of the alveoli.

Many of them are distinctly thickened through increase of fibrous tissue, which is, generally speaking, very homogeneous-looking and very translucent; this is specially noticeable under the thickened pleura.

E. *Heart and pericardium.*

The heart was small, and weighed 7 oz.; it was contracted, and felt very firm; its cavities contained a few small pale clots, and were apparently normal; there were no valvular lesions. The pericardium contained a slight excess of greenish-yellow serum.

F. *Gastro-intestinal canal and peritoneum.*

There was no trace of peritonitis. The serous coat of the intestine and stomach was smooth, and looked healthy. The mucous membrane seemed quite healthy as far as the lower part of the ileum. The lowest part (twelve inches) of the *ileum* was congested. There were also in that region numerous small nodules closely resembling swollen solitary glands. Peyer's patches were not specially affected.

The cæcum, the *ascending* and *transverse* parts of the colon were much ulcerated. Sixteen large ulcers were counted at the time of the *post-mortem*, but numerous small ulcers and swellings were also observed. The distribution of the large ulcers was as follows:

Three were found two inches beyond the ileo-cæcal valve; one large compound one, evidently resulting from the coalescence of smaller ones, 4 inches beyond the ileo-cæcal valve; six medium-sized ulcers, 16 inches beyond the ileo-cæcal valve; six medium-sized ulcers, 28 inches beyond the ileo-cæcal valve.

Of these ulcers, those which seemed not to have been produced by the coalescence of a number of small ones measured from $\frac{1}{8}$ to $\frac{1}{2}$ inch in diameter or a little more.

They were mostly round or oval, and they all seemed to have begun in small nodular swellings similar to those found in the small intestine. Owing to these the smallest ulcers were raised above the level of the mucous membrane, and when a little larger they had a raised but soft border, not undermined. The bottom was generally not very rough, and often quite smooth. Some of the larger ulcers had, however, some distinct granular or tubercular-looking nodules near their border. The intestinal walls were not much thinner than normal at the level of the ulcer, the ulceration apparently not extending much beyond the mucosa, the muscular coat never being exposed or even affected. The serous coat seemed also free from disease.

Microscopically.—The lesions seem to be chiefly due to a large accumulation of small round-cells in the mucous membrane of the intestine. These cells do not extend very far into the submucosa; they at first occupy the spaces between the Lieberkühn's follicles, of which they cause wide separation and rapid atrophy. In the lesions which have not yet ulcerated it is difficult to find any bacillus. In the ulcerated ones bacilli are found abundantly among the granulation cells and the granular *débris* forming the bottom of the ulcer. These bacilli are much more easily decolourised than those found in the skin, but they do not differ from the discrete ones in form or general appearance.

Among the cells surrounding the ulcer there are some giant-cells which, as in the laryngeal lesions, seem in many cases to have originated in lymphatic vessels. These cells do not seem to form part of any granuloma resembling a miliary tubercle. The blood and lymphatic vessels in the neighbourhood of the lesions were searched for bacilli without any positive result.

G. *Liver.*

This organ weighed 52 oz., and was unaltered in shape, rather pale, and very firm. Its surface was smooth. The capsule seemed more opaque than normal, and presented a fine mottling, which on section of the organ was seen to correspond to a general increase of stroma, and gave to the organ a most typical appearance. Small dots and lines, resembling much the trabeculæ of the spleen, and giving to the surface of section a shreddy appearance, were distributed evenly all through the organ. The dots were smaller than miliary tubercles.

Microscopically.—The liver is found to be in a state of advanced and very general interstitial hepatitis. Glisson's capsule is generally increased, and presents nodular swellings of fibrous tissue, in which a great number of large and small vacuolated cells are found around the blood-vessels and between the bile-ducts. The bile-ducts seem increased in numbers, and are very conspicuous; some are obstructed by shed epithelial cells. These lesions are very similar to those of biliary cirrhosis, but the fibrous tissue is different in appearance, owing to the large number of vacuolated cells looking much like fat-cells. The hepatic cells are either in a state of proliferation, or are infiltrated with fat; many are much atrophied.

Bacilli are found in the vacuolated cells of Glisson's capsule, more especially around the blood-vessels, and evidently situated in lymphatic spaces. They are also pretty often found between the liver-cells in the midst of the lobules, where they seem to be within or sometimes outside the blood capillaries. Bacilli are also found all through the thickness of the walls of even pretty large portal veins, surrounded by large masses of bacilli; the same is not true of the branches of the hepatic artery. The bacilli are generally short, very granular, do not stain so readily or so deeply as those of the skin, nor do they retain the stain so well; they have also by keeping lost their affinity for carbolised and anilined fuchsin to some extent. (This loss has not been noticed yet in the skin.)

H. *Spleen.*

This organ was enlarged, weighed 12 oz., and was flabby but not softened. Its appearance was very similar to that of the liver; a number of small whitish shreds or granules were found disseminated uniformly all through the pulp. These whitish bodies had a fibrous, shreddy appearance. The largest among them was smaller than even small miliary tubercles. The organ felt somewhat nodulated, but with the exception of a small cheesy nodule measuring about $\frac{1}{12}$ inch in diameter no distinct nodule could be seen with the naked eye.

Microscopically.—There is a general increase of stroma. The trabeculæ and many of the arteries have at their sides masses of large vesicular-looking cells, resembling the small leprous cells found in other organs. There are numerous patches of necrosed tissue, not exactly cheesy-looking, but almost entirely structureless, and composed of granular and hyaline products. Around these patches numerous giant-cells are found. Some of these giant-cells are formed in some of the sinuses or lymphatic spaces of the pulp. Some of the sinuses are lined with a layer of epithelioid cells, giving to certain parts of the organ a glandular appearance. Many of the arteries are much sclerosed, and are almost entirely obliterated by their intima.

Bacilli are found abundantly around the trabeculæ and the arteries, and some of the Malpighian bodies have groups of them in their centre around the artery. (Most Malpighian bodies are, however, indistinct.)

Bacilli, free or in vacuolated cells, are also found forming small groups in the midst of the pulp.

The cheesy masses do not contain bacilli, but some of the giant-cells surrounding them (and having to them the same relations as the pulmonary giant-cells have to the corresponding cheesy nodules) contain a few bacilli, some even containing small colonies, and resemble leprous cells. This seems, however, to be accidental, as the giant-cells appear to be specially connected with the cheesy nodules, and not with the lesions containing the typical groups of bacilli. In the spleen, as in the liver, the bacilli are rather short and granular; they stain well, but slower than those of the skin.

I. *Genito-urinary organs.*

The *kidneys* weighed together 9 oz. Their capsule stripped off easily; the cortex was pale, the boundary layer congested. The *urinary passages* and *bladder* were healthy-looking.

Microscopically.—The convoluted tubules were found to be in a state of cloudy swelling at places, and of catarrhal desquamation in others. There was congestion. No bacilli could be found in the parts which were examined.

(*Testicle.*—The examination of that organ was accidentally omitted.)

K. *Supra-renal bodies.*

They seemed to the naked eye to be healthy. On microscopical examination it was found that there was much atrophy of their cortical epithelium, and proportional increase of the interstitial fibrous tissue. No bacillus could be discovered.

L. *Thyroid body.*

This organ was small and apparently normal. On microscopical examination it was found that all the alveoli contained a large amount of colloid matter. The interstitial tissue was normal in amount. No bacillus could be discovered.

M. *Lymphatic ganglia.*

The lymphatic ganglia were swollen and altered in colour in various parts of the body. The cubital ganglion at the bend of

the elbow, the lymphatic glands at the root of the neck, in the posterior mediastinum and around the bronchi, and also some of the mesenteric glands were swollen. The ganglia which seemed most affected were the cubital and the cervical glands. The cubital ganglion measured nearly 1 inch in length and $\frac{3}{8}$ inch in width. It was firm, brownish grey in colour, and seemed to be in a state of chronic inflammatory induration. The glands at the root of the neck were much softer, congested, mottled, and they were generally arranged in pretty large clusters. There were numerous small rounded whitish nodules, generally smaller than miliary tubercles, all through the substance of these glands.

Microscopically.—The cubital ganglion is found to be in a state of chronic interstitial inflammation, as indicated by the presence of much fibrous tissue, chiefly in the central parts of the gland, but also in the capsule. Very few patches of typical lymphoid cells can be found, and no distinct follicle can be discovered.

The blood-vessels are much congested. Numerous oval, elongated and branched spaces are found, chiefly under the capsule, which look like dilated lymphatic channels, corresponding to the sinuses of the organ. In these cavities large vacuolated bodies, resembling closely the leprous cells of the skin, are found. Some are of very considerable size. Many show a large central vacuole and several peripheral ones. In some of these vacuoles a body staining more or less distinctly like a nucleus is sometimes visible. In some cases a layer of protoplasm containing nuclei forms a crescentic margin on one side of these vacuolated bodies. The lymphoid cells are, in other parts of the ganglion, replaced by swollen, translucent, vesicular, epithelioid cells.

An immense number of bacilli are found all through the organ. In the large leprous cells they are so abundant that it is difficult to differentiate them. They are, however, quite clear and discrete in the small epithelioid cells. They have in the ganglion the same relations to cells and lymphatic spaces as in other parts of the body, but if anything they are more abundant.

N. Nerves.

Many of the cords entering into the formation of the *brachial*, *lumbar*, and *sacral* plexuses were examined, and seemed to the naked eye to be healthy. The *ulnar nerves* could, however, be

clearly felt through the skin to be much thickened in the region of the inner condyle of the humerus, and they were, therefore, examined. Several other peripheral nerves must have been affected, but they were not dissected out.

The *right ulnar nerve* was swollen and indurated over a length of about half an inch in the region just indicated; it was not, however, discoloured in the least, nor was it adherent to any of the surrounding tissues.

The *left ulnar nerve* was much more thickened, the swelling measuring at least one inch in length. The nerve was also much discoloured by congestion in that region. It looked healthy above and below the swelling.

Microscopically.—The lesions were clearly those of chronic interstitial neuritis, with considerable inflammatory changes in some of the nerve-fibres, and considerable atrophy of others. The fibres were, however, very unequally affected.

Bacilli were found abundantly in all the parts where lymphatic vessels or spaces could be present. In some cases the bacilli seemed to have penetrated into the nerve-fibres themselves. It was, however, found difficult to decolourise entirely the myelin sheath without decolourising a great proportion of the bacilli, and it is possible that the network of neuro-keratin may have in some places simulated bacilli.

IV. DISCUSSION OF THE CASE.

A. *General remarks.*

This case presents features of interest in the history of the disease.

The patient was born of English parents in India, and presented no symptoms of disease until the age of sixteen, when, a few months after returning to India, from which he had been absent in England for nine years, he became rapidly leprous. It is noticeable that he returned to a district where leprosy was common, and that he suffered from well-marked fever during the appearance of the lesions which probably indicated the onset of the disease. It may be noticed that these lesions, as Hutchinson has remarked in many cases, were symmetrical. It is also evident from the history that the appearance of the cutaneous lesions was accompanied by fever.

The case also afforded us an opportunity to make some observations during life. We both attempted to demonstrate bacilli in the *blood* and *lymph*, obtained by compression of non-ulcerated tubercles, according to the methods recommended by some observers. Although a very large number of preparations were examined we failed to find any bacilli in the fluids thus obtained from lesions which, after death, were found to be absolutely crowded with bacilli.¹ The same reagents were used for demonstration both before and after death. We conclude, therefore, that, notwithstanding the positive results obtained by these methods by other observers in other cases, it is advisable, in order to demonstrate the bacilli, to remove a small portion of skin. The smallest portion of skin removed from a part where there is any indication of a lesion will suffice. We do not, of course, pretend that bacilli cannot be demonstrated in the blood, lymph, or serum of leprous lesions, but only that their presence is certainly not constant. Beaven Rake, in his examinations of various materials, and especially the juice squeezed or scraped from fresh tubercles, was able to demonstrate the bacillus in 33 per cent. of the cases examined. We inoculated all the usual nutrient media with the fluids just mentioned. Whenever the lesions were not ulcerated we obtained no growths whatever. With ulcerated lesions we obtained simply the usual organisms found in open wounds. These results are not surprising in the light of what has just been said about the absence of bacilli and the results of *post-mortem* examination. When the disease presents the characters recorded here, blood, lymph, and serum do not afford suitable materials for inoculation experiments. In this we agree with the general experience. We do not wish to attract special attention to the mode of origin of the various lesions, although many of the histological features are very suggestive; neither will we attempt to discuss the mode of spread of the bacilli. It is to a discussion as to the nature and relations of the pulmonary lesions that we wish to confine ourselves, and more especially to the inquiry whether the lungs were in a state of tubercular or leprous phthisis.

¹ We are informed by Dr. Payne that while the patient was at St. Thomas's Hospital similar attempts to demonstrate the bacillus in blood and serum were equally unsuccessful.

B. *Nature of the lung lesions.*

a. *Evidence of various observers.*—The great frequency with which leprosy ends fatally, owing to the lungs being affected by pneumonia or phthisis, has struck all who have had to deal with the disease. As to the nature of this special pneumonia or phthisis, the older observers express no doubts, but regard it as ordinary broncho-pneumonia on the one hand, or tubercular phthisis on the other. The lesions of the intestine also, which are associated with the dysenteric diarrhœa so frequently found in fatally ending leprosy, were similarly considered as due to some associated disease, such as tuberculosis or dysentery, and not to leprosy.

Danielssen and Boek consider the lungs of lepers as almost always free from infection, though they admit that the bronchi and bronchial glands are attacked by the disease. The pleuræ, too, are frequently affected by what they admit is leprosy, but the underlying lung is usually found healthy. According to these observers, then, there are present leprotic lesions of the bronchi, bronchial glands, and pleuræ, while the parenchyma of the lung escapes. Similarly they admit a leprous affection of the mesentery and mesenteric glands, though apparently they except the intestinal lesions.¹

Leloir, while commenting on the large number of lepers who are phthisical or scrofulous, or of phthisical or scrofulous families, considers that the lungs are almost always free from leprosy. In only two cases has he found bacilli in the lungs. One of these he describes as tubercle, and the other as broncho-pneumonia.

Hansen, from 100 *post-mortems*, concludes that there was no case in which the lungs, intestines, serous membranes, or kidneys were affected by leprosy. He regards all the affections of these organs or membranes as tubercular.

Neisser, Virchow, and Köbner also regard lung leprosy as doubtful. On the other hand, from his observation in Hawaii, Arning came to the conclusion that the pneumonia and phthisis of lepers must be regarded as integral parts of the original disease, and as truly leprous as the affections of the skin.

Bonome also in two cases of leprosy, from one of which Uffreduzzi's cultures were made, considered that the lung affections were true leprosy. This latter observer bases his opinion on the characters of

¹ Danielssen and Boek, English translation, p. 212, &c.

the lesions and of the bacilli so far as regards the staining reactions and distribution, but did not make any inoculation experiments. In his cases the lesions of the larynx and trachea were practically similar to those we have described above.

The bronchial glands were affected in the same way also. The bronchial mucosa was infiltrated with small cells and covered with slimy exudation. There was a general state of broncho-pneumonia, and of "peribronchitic induration." In all this our case agrees with his. He, however, describes the pleuræ as thin and transparent, and the lungs as small, pigmented, hard, and nodulated. In the present case the lungs were undoubtedly indurated, nodulated, and pigmented, but they were large. We also agree in great part with him as to the distribution of the bacilli and as to their character. He found them chiefly in the bronchial secretion, but also in the small-celled infiltration of interalveolar septa, where we, on the contrary, found them extremely seldom. (It is true that on fresh sections, stained immediately after the *post-mortem* examination, one of us saw around vessels contained in interlobular septa quite typical clumps of bacilli identical with leprous cells in other parts of the body; the stain of these sections has, however, faded, and no other section has been obtained showing the same appearance since, so that we do not insist on this.) Bonome also describes thick masses of bacilli in the hyaline zone. These masses correspond probably with those which we have ourselves observed in the midst of the decayed bronchial products, which are very hyaline, and surrounded by granulation tissue containing giant-cells. The bacilli are described as shorter and thicker than the *Bacillus tuberculosis*.

Perhaps the most valuable contribution to the subject is a posthumous paper by Damaschino describing two *post-mortem* examinations of lepers. In one of these cases the lungs seemed to be really affected with tuberculosis.

Histologically at least the lesions were similar to those of chronic tuberculosis, and it is interesting to note that in that case the skin contained also distinct giant-cells in the midst of leprous nodules. There was also more or less extensive ulcerations of the mucous membrane of the intestine.

In the other case the lungs were heavy and large. There were pleural adhesions, and cavities varying in size from that of a pea to that of a walnut. The lungs contained a number of typical

tubercles, giant-cells, caseous masses, and a considerable number of bacilli, short, felted, and absolutely similar to those of the liver and spleen (which organs were typically leprotic). There were also a few isolated or clumped bacilli, which from their length and thinness seemed to be tubercular bacilli. Inoculations in series demonstrated the existence of tubercular bacilli in the lungs, but Damaschino thought nevertheless that the main cause of the lung lesions was leprosy. Commenting on the case, Damaschino says that inoculation proves conclusively the existence of a pulmonary tuberculosis, whose bacilli are lost in the midst of leprosy bacilli. It is interesting to note that in this case there was distinct sub-peritoneal tuberculosis of the intestine. In our case, on the contrary, there was no evidence of anything like a tubercle anywhere in the intestine, and the peritoneal coat was perfectly smooth everywhere.

There is obviously considerable difference of opinion as to the nature of the pulmonary lesions in leprosy, and the weight of the opinion is, it must be confessed, adverse to the existence of leprosy phthisis. It must, however, be remembered that some of the facts are susceptible of a different interpretation.

Statistics do not prove much, but such as exist seem to show a connection between phthisis and leprosy greater than would be expected if they were merely intercurrent independent diseases.

β. Statistics.—The figures available for determination of the percentage number of deaths from phthisis in lepers is not very large, but they all point to the extreme frequency of the disease. Hillis, in British Guiana, says that in tubercular leprosy, deaths from lung complications, including phthisis, amount to 17 per cent. of the total deaths. The percentage of deaths among the general population of British Guiana from phthisis is 7·1 per cent.

In the leper hospital at Kakaako, in Hawaii, the percentage of deaths due to what is variously registered as phthisis, consumption, and tuberculosis, amounts to 21·8 per cent. The percentage of deaths from phthisis to deaths from other diseases in the district of Rona, which includes Honolulu, and with which the death-rate of Kakaako may be compared, is from 11·2 per cent. to 12·5 per cent.

In the carefully kept Hospital Reports of the Trinidad Asylum, compiled by Beaven Rake, the percentage of deaths recorded as due to phthisis, and total deaths for the years 1885 to 1889, are—

	Total deaths.		Phthisis.		Per cent.
1885	...	28	...	7	25
1886	...	21	...	3	27·6
	(in only 11 cases cause recorded)				
1887	...	30	...	7	25
1888	...	16	...	6	37·5
1889	...	16	...	3	12·5
In 5 years total deaths . 111					
Deaths from phthisis . 26 = 23·4 per cent.					
Excluding 10 unrecorded . = 25·7 „					

It is instructive to compare the number dying of phthisis with the number suffering from phthisis in the hospital.

	Deaths from phthisis.		Recorded as phthisical.		Total lepers.
1885	...	7	...	9	173
1886	...	3	...	7	168
	(10 unrecorded)				
1887	...	7	...	6	236
1888	...	6	...	6	167
1889	...	3	...	10	225

It would seem, then, that the phthisis is rapid and extremely fatal. In the present case the patient is recorded as presenting no definite physical signs of consumption at the end of August, 1888, though he had had cough and night sweats for a few weeks; but by May, 1889, and indeed earlier, he had signs of advanced phthisis, and died in July, 1889, with pneumothorax.

Turning to the intestinal lesions, it is seen that diarrhœa, associated or not with ulceration of the intestine, is also the cause of many deaths in cases of leprosy. Thus Hillis gives the percentage of deaths from diarrhœa in cases of tubercular leprosy as 10 per cent., and in anæsthetic leprosy at as much as 36 per cent. In the latter variety of the disease it takes the form of a mucous enteritis.

In the Kakaako Hospital, again, diarrhœa caused 6·2 per cent. of the total deaths. The statistics of the Trinidad Asylum show that diarrhœa was a common intercurrent affection.

Date.		Total cases.		Percentage who suffered from some form of diarrhœa.
1885	...	173	...	10·9
1886	...	168	...	13·6
1887	...	236	...	12·2
1888	...	167	...	21
1889	...	225	...	17·7

It is to be noticed that in all the *post-mortems* recorded above ulceration of the intestine was present.

Though, as stated above, the weight of opinion is against the idea of leprosy affecting the lungs, still the facts above related show that it is admitted—

1. That lung affections are very common indeed in leprosy (18 per cent.—21·8 per cent.—25·7 per cent.), and that ulceration of the intestine and diarrhœa is also extremely frequent.

2. That though the lungs are said to be affected by tuberculosis, it is admitted that the pleuræ, bronchi, and bronchial glands are the seat of leprotic lesions.

3. That while the skin and internal organs are admittedly leprous, the lungs are affected by a different disease.

4. That finally the lungs may be the seat of tuberculosis though crowded with the parasite of leprosy.

It certainly seems remarkable that the lungs should possess such a curious immunity from leprosy, and alone of all the organs escape, when at the same time they are affected so often by a disease which, in the character of the lesions produced and the micro-parasite found, so closely resembles leprosy.

γ. *Our own observations.*—In order to elucidate, if possible, this question we undertook a series of investigations, which had for objects the study of—

1. The value of the various criteria which are used to differentiate the bacilli of tubercle and leprosy.

2. The distribution of the *Bacillus lepræ* in the tissues of various organs.

3. The effects which the place of growth has on the characters of the bacillus.

4. The nature of the lesions.

1st. *Value of various criteria.*—While all observers agree as to the close resemblance in size and shape between the two bacilli, yet the measurements given are not always in accord with this

statement. This is scarcely surprising if the extreme variability of the *Bacillus tuberculosis* as it occurs in sputa, in culture, and in internal organs is remembered. Flügge and others give for *Bacillus lepræ* measurements nearly double those given by Koch for *B. tuberculosis*, while Bonome and Damaschino speak of the former bacilli as shorter and thicker than the latter. Similarly with regard to shape, the general opinion is that *B. lepræ* is more uniform and more rectilinear, but Baumgarten failed to establish any decided differences; and while Neisser regards the pointed extremities of *B. lepræ* as characteristic, Bordone Uffreduzzi draws attention to the terminal swellings of the same bacillus.

There is a conflict of opinion as to the motility or non-motility of the *B. lepræ*. Both bacilli are described as possessing a gelatinous envelope (*B. lepræ*—Neisser, Unna, Lutz, Babes; *B. tuberculosis*—Koch, Lutz, Unna).

With regard to staining reactions, also, the similarity between the two bacilli is much more striking than the differences; and a comparison of the various opinions expressed by investigators leads to the conclusion that, contrary to the original idea, any stain which will give results with the *B. lepræ* will also stain the *B. tuberculosis*. Successive authors have drawn up lists of differential stains, which usually show that some will stain *B. lepræ* while leaving *B. tuberculosis* unstained. The statements of one observer are, however, almost always traversed by the positive statements of another; and whatever may be the cause of these discrepancies, it is obvious that such contradictions entirely deprive of weight any opinion as to the nature of the bacilli based on these grounds. Both the *B. lepræ* and the *B. tuberculosis* are stated by one or more investigators to be stained by concentrated watery, or dilute alcoholic solutions of fuchsin, safranin, gentian violet (and its varieties), methyl violet, dahlia, malachite green, and methyl green. With regard to methylene blue, the statements are flatly contradictory. Babes recommends it to stain *B. lepræ*; Baumgarten says that neither watery nor alcoholic solutions of this dye stain either bacillus; and Wesener, while agreeing with Baumgarten, adds that dilute alcoholic alkaline solutions stain both *B. tuberculosis* and *B. lepræ*.

The discrepancies arise in part, undoubtedly, from the varying properties of the stains used; but sufficient weight does not appear to have been allowed, though the cause is recognised, to the variations of the bacilli in different cases. Our own experiments lead us

to the opinion that the staining reaction varies not only in different cases, but in the various organs of the same case.

Another source of discrepancy may arise also, in that it is by no means easy to decide, when using such stains as Löffler's blue, simple methylene blue, or even Bismarck brown, whether the bacilli in sections are stained or not. The leprous cells are mapped out by the stains, and traversed by faint granular lines which seem to correspond with the bacilli seen in sections stained by more suitable dyes, but it would be impossible to recognise individual bacilli. Alkaline methylene blue, however, in some cases, and notably the affected nerves, stained individual bacilli well and strongly.

The *B. lepræ* is also stated to be more rapidly coloured and less rapidly decolourised than *B. tuberculosis*. The most definite statements are those of Baumgarten, who has arranged a differential method which, though probably useful, cannot be relied upon in diagnosis of the two bacilli. According to him, dilute alcoholic fuchsin (5—6 drops in small watch-glass of water) stains *B. lepræ* (in sections) in 12—15 min., so as to resist $\frac{1}{2}$ min. in acid alcohol (absolute alcohol 10 + HNO_3 1). *B. tuberculosis* under these circumstances remains unstained. On cover-glasses 5—6 min. is the time necessary to stain *lepræ*.

We find that by Baumgarten's method several varieties of fuchsin unmistakably stain the *B. tuberculosis* as well as the *B. lepræ*; and, indeed, we found that so short a time as six minutes was sufficient, in cold concentrated watery rubin, fuchsin, or magenta, to definitely stain the *B. tuberculosis* in tissues. It is admitted that different samples of stain vary much in their properties. It must be understood that it is not denied that if sections of tubercle and leprosy are stained thus rapidly, a much larger number of bacilli will be seen in the leprosy sections than in those of tuberculosis. This, however, depends not upon the different staining reaction of the two bacilli, but upon the fact that the bacilli are present in so much greater numbers in leprosy. It is a distinction based really on the number of bacilli present, and not on any essential difference in the reactions of the two bacilli. Besides these methods of Baumgarten, there is one suggested by Lustgarten, based on rapidity of decolorisation by hypochlorite of sodium; and methods by Voltolini, Unna, and Lutz, based on the production of a streptococcus-like form, in the first case in

B. tuberculosis, and in the second in *B. lepræ*. In many organs, however, the non-bacillary form is chiefly found in any method of staining.

The picture presented by leprosy sections stained with fuchsin by these rapid methods, compared with that obtained by prolonged staining, is very suggestive. In the latter case the most striking objects are the large red leprous cells visible with a low power. In the former case these cells are no longer conspicuous, and, indeed, usually present, on examination with a high power, one or two red bacilli only in a mass of material stained with the counter-stain. A very large proportion, however, of the bacilli found either between the cells or in the small epithelioid cells are stained well. This would seem to indicate that the bacilli in the two situations are in very different conditions.

It is obvious, then, that, so far as the size, shape, and staining properties of individual bacilli are concerned, it is impossible to distinguish between the *Bacillus tuberculosis* and the bacillus of leprosy by any of the criteria proposed.

2nd. *Distribution of the Bacillus lepræ*.—Generally speaking, the most uniformly affected part of the body was the skin. The mucous membrane of the mouth, pharynx, and larynx was involved very much in the same way. Bacilli were extremely abundant in these parts. Many terminal nerves and some nerve-trunks were affected as deeply as the skin; but, if one may trust a naked-eye examination, none, or at any rate few, of the large cords forming the various great plexuses of spinal nerves showed any leprotic lesions.

Some lymphatic glands also contained a prodigious number of bacilli, but in others the bacillus could not be found, although the ganglia were much diseased. The bacilli were also very abundant in the Haversian canals and spaces, and in the marrow of the phalanges, which were the only bones examined microscopically.

In this connection it may be remembered that Uffreduzzi's cultivation was made from the marrow of bones, and that, referring to this culture, Kaurin states that he has never observed bacilli in bone marrow.

The organisms were also present in the liver and spleen, but less abundant in these organs than in the skin. Certain organs—the kidneys, the supra-renal bodies, and the thyroid—seemed entirely free from them. The mucous membrane of the stomach

and small intestine, as well as that of the bladder, seemed also to be quite free from disease.

In many lymphatic spaces and blood-vessels the endothelial cells contained a large number of bacilli. In some cases these cells seemed to coalesce, and give rise to the large leprous cells with central lumen to which we have alluded in several places. Babes has also described bacilli in the endothelium of blood-vessels.

If, instead of taking the distribution of the bacilli in organs, we consider the relation to tissues, a number of interesting facts are brought out. The tissue most affected is undoubtedly the ordinary *loose or areolar fibrous connective tissue ; then the lymphoid tissue*. In the areolar connective tissue the bacilli are almost without exception either apparently free in lymph spaces or vessels, or, what is more common, embedded in small epithelioid cells, accumulated in lymphoid spaces, or in large masses generally described under the name of leprous cells. Fixed connective-tissue corpuscles, apparently compressed between fibrous bundles, are also affected, but when this is evident the bacilli are few and the lesions slight. In the *lymphatic tissue* the bacilli have pretty much the same relations. Many small, round, lymphoid cells or leucocytes are also distinctly affected. The *adipose tissue* of the subcutaneous layers, and of the marrow of bone, is much affected. *Dense fibrous tissues*, such as tendons, are very little involved; what looks like a tendon-corpuscle here and there contains a few bacilli; the same may be said of bone-corpuscles.

Hyaline, fibro-, and elastic cartilages remain perfectly free from bacilli, even when surrounded by them in all directions. It is, therefore, evident that the connective tissues are, with the exception of the densest forms, much affected, and that the number of bacilli is very nearly proportionate to the size of the lymphatic spaces in which they are lodged.

The *epithelial tissues* are, generally speaking, free from bacilli. Here and there a few bacilli, however, penetrate into the deep layers of the rete Malpighii of hair follicles and of sebaceous glands. They may even pass towards the surface of the skin with the sebaceous secretion: a few have been found in the acini and ducts of mucous glands. They, however, do not thrive in epithelial cells, and no large colony has been found in any epithelial tissue.

Monastersky and Neisser affirm that the epithelial layers do not contain bacilli; and in this they are confirmed by Cornil and Suchard; but subsequent observers—amongst them Thin and

Babes—have described them in epithelial structures, and chiefly in those mentioned as showing them this case.

The sweat-glands are free according to Babes, Unna, and Touton. We also were unable to detect any bacilli in their epithelium, but were struck with the extraordinary accumulation of bacilli around most of them, or rather in the fibrous tissue which so frequently almost entirely replaces them.

In *nerves* they are found abundantly in the lymphatic spaces and connective-tissue corpuscles, and in some cases they seem to have penetrated into and grown in the myeline sheath.

In *non-striped muscles*, such as those entering in the sheath of arteries, bacilli may be found pretty abundantly in small round masses and in small groups of two or three; they seem, however, to lie generally between the fibres.

In *striped muscles* they are found pretty abundantly in the endomysium and perimysium, and in some instances a few have penetrated into the muscular fibre itself.

Generally speaking, therefore, the bacilli seem to grow well only in the lymphatic spaces of loose or moderately loose connective tissues, whether these tissues form continuous tracks as in the skin, or enter into the formation of organs such as nerves, muscles, or glands.

There is, however, a feature worth noticing. Wherever the connective tissues become exposed by shedding of the epithelium covering it and ulceration, the bacilli seem to disappear entirely or in part; they do not at least respond any more to the ordinary tests. It is only when they seem to be multiplying with great rapidity, or when the ulcerative process is very active, that bacilli are found in the superficial products; but even then they are much less abundant than in the corresponding parts which have not ulcerated.

The number of bacilli found in various organs or lesions is, therefore, not only determined by the functions and relations of the organ, but also by the form of connective tissue entering into its composition, and probably also—at least so far as demonstration is concerned—by the amount of shelter from the air afforded by superficial layers of epithelium.

In respect to exposure to air, the lung parenchyma is comparable to the skin or a mucous membrane deprived of its epithelium, and therefore, on this supposition, the bacilli should not be easily demonstrable by the usual methods.

When large cheesy masses are found in the lungs the central portion of them is far removed from the contact of the air, and here we find large masses of bacilli.

The mucous membrane of the air-passages, which is comparable to intact skin, is also one of the places where bacilli are generally easily shown.

We mention the *apparent effect* of exposure to air for the purpose of generalising the facts which we have observed in the skin and mucous membrane, where, by ulceration, the epithelium had been removed. In those places bacilli, which were extremely abundant in the tissues immediately surrounding the lesion, were not to be demonstrated, except occasionally in small number, by the ordinary methods. We have no proof whatever that this is due to the action of air, but this seemed to be the only general connecting relation between the parts where bacilli could not be brought out by staining, although one would have expected them to be abundant.

3rd. *Variability of the characters of the bacilli according to their distribution in the body.*—This variability was really the first thing which attracted the attention of one of us to the very unsatisfactory state of our knowledge of the characters of the *Bacillus lepræ*.

(1) The discrete bacilli, or those contained in small epithelioid or lymphatic cells, differ in characters from those contained in the so-called leprous cells as follows :

Discrete bacilli.

1. Are generally short, though distinctly bacillary.
2. Stain quickly.
3. When well stained are comparatively easily decolourised.
4. Take a brighter and somewhat more transparent colour with fuchsin.
5. Are much more clearly defined, owing to the surrounding substance not staining or being decolourised.
6. Prolonged steeping in acid alcohol renders them more refractory to staining (bone).

Bacilli in leprous cells.

1. Generally very long, and pretty often beaded.
2. Stain more slowly.
3. When well stained retain stain vigorously.
4. Take a deeper and more opaque stain.
5. The interbacillary substance stains deeply, and is difficult to decolourise.
6. Prolonged steeping does not prevent staining to any serious extent.

(2) On the day of the *post-mortem* examination numerous fresh

sections were cut and left in cold fuchsin for five minutes, fifteen minutes, two or three hours, twenty-four hours, and forty-eight hours. In the case of nearly all the organs examined the first trial (five minutes) gave very unsatisfactory results or none. The second (fifteen minutes) gave invariably good results with the skin. The third experiment (two to three hours) gave good results with the skin, nerves, and lymphatic glands, but imperfect with the liver, spleen, lungs, and intestine, specially with the last two organs. The fourth and fifth trials gave good results with every organ. These experiments were made in summer at a temperature of about 18° to 20° Centigrade.

The bacilli contained in various organs can, therefore, be said to vary in their reaction to staining reagents. The following table gives a summary of the results obtained on various occasions.

They stain rapidly and well, and are not easily decolourised in the	They stain more slowly and are more easily decolourised in the	They stain well in the
Skin.	Liver.	fresh tissues, but lose this property to some extent when kept in absolute alcohol in the
Mucous membrane of larynx.	Spleen.	Liver.
Nerve.	Intestine.	Spleen.
Lymphatic gland.	Bone? (bones had been decalcified).	Intestine.
		In the liver and spleen they still stain well after two years, but they have lost their distinct bacillary form, and look very beaded.

(3) Their appearance varies in the different organs.

They are long, or at least very distinctly bacillary in the	They are shorter or more generally beaded or granular in the
Skin.	Liver.
Mucous membrane of larynx.	Spleen.
Nerve.	Bone.
Lymphatic gland.	Muscle (almost like cocci; they are also very thick, and stain extremely deeply).

From these very general statements it is evident that but little value can be attached to the characters of the bacilli in determin-

ing whether a lesion is tubercular or leprotic. No serious objection on this ground can, therefore, be raised against our regarding the bacilli in the lung as being quite as likely to be leprous as tubercular.

4th. *Nature of the lesions.*—There can be no doubt as to the existence in this case of extensive broncho-pneumonia, combined with an interstitial pneumonia of a peculiar type, owing to the presence of an unusual number of epithelioid cells in the interstitial tissue. It is also evident that no true miliary tubercle nor even a typical cheesy tubercle can be found anywhere. The giant-cells found at the periphery of some of the cheesy-looking masses, resulting from the necrosis of pneumonic products, have not the usual characters presented by those found in tuberculosis. They have connections very similar to those of giant-cells found in the larynx and the spleen, both of which organs present most typical leprotic lesions.

The lesions have the same characters as those observed in other organs, such as the skin for instance. These lesions consist of congestions, accumulations of peculiar translucent vesicular-looking epithelioid cells in the lymphatic spaces, necrosis of tracts of tissues, degeneration of all the epithelial structures, which become surrounded or undermined by leprotic cells; consecutive fibrous induration, and atrophy. Such lesions are certainly found in cases of ordinary tuberculosis, but they rarely if ever attain the general characters observable in this case, and they are generally combined with more typical lesions.

If such lesions were found in a case of undoubted tuberculosis, one would feel inclined to consider the case as one of tubercular cheesy pneumonia presenting unusual features.

Under such circumstances, is it wise to insist upon the tubercular nature of the pulmonary lesions? No; unless one were prepared to consider leprosy as a peculiar variety of tuberculosis, a view which is perhaps not so unlikely to be true as one might fancy at first.

V. GENERAL CONCLUSIONS.

From all this we conclude—

1st. That the *tests* proposed by various writers for distinguishing the *Bacillus lepræ* from the tubercular one are insufficient.

2nd. That the *characters* of undoubted *Bacilli lepræ* are so

variable that there are as great differences between two extreme forms of this organism as between what are considered by authors to be typical bacilli of tuberculosis and leprosy.

We do not feel therefore justified nor inclined to decide whether the bacilli found in this case were tubercular or leprous on such grounds.

3rd. That the *distribution* of the bacilli revealable by usual staining methods is such that organs like the lungs would, if affected with leprosy, present lesions differing from those occurring in other organs, and that the free access of air seems to be against the bacillus retaining the characters under which we know it.

4th. That the *lesions of the lungs* are more closely allied to those of the other leprous organs than to those of ordinary tuberculosis; and that in presence of the abundance of the bacillus of leprosy in nearly every part of the body, and indeed in the air-passages and pleura, it is somewhat illogical to try to find another cause for the existence of these lesions.

The only test which can be of use in determining this question finally is inoculation; and if the results already obtained by Damaschino should be obtained in all cases in which the lungs are affected thus, it would be well to reconsider the whole question, as to whether leprosy may not be some very modified form of tuberculosis *which, when virulent enough to involve certain organs, such as the lung, tends to revert to the form with which we are best acquainted.* In favour of such a view, we would simply urge the following points, without, however, wishing to pledge ourselves to such a conclusion.

1st. The characters of the bacillus and its staining reactions.

2nd. The nature of some of the lesions.

3rd. The frequency of phthisis and scrofula in leprous patients (over 25 per cent.) or in their antecedents.

4th. The difficulty of obtaining any result from inoculation with the most typical and advanced leprotic lesions.

5th. The success of inoculation with products obtained from organs less typically and frequently affected, such as the lungs.

6th. In cases of successful inoculation the production of a disease which is generally tuberculous, or indistinguishable from tuberculosis.

To prove the correctness of this supposition, it would be necessary

to discover cases in such stages, or under such conditions, that the bacilli obtained from various parts of the body were capable of producing tuberculosis by direct inoculation or after cultivation. Until it has been proved that it is possible to reproduce leprosy by the inoculation of the *Bacillus lepræ* we think there is not more evidence in favour of the view that the lesions of the lungs are not leprosy because they give rise to tuberculosis, than in support of the one that leprosy lesions are the results of a *modified form of tuberculosis which tends to return to the normal type in the lungs*.

May 23rd, 1891.

VI. BIBLIOGRAPHICAL APPENDIX.

1. Arning.—'Virch. Archiv,' Bd. xcvii. 'Report on Leprosy to Board of Health,' Honolulu, 1886. 'Journal of Leprosy Committee.'
2. Babes.—'Les Bacteries,' 2nd edition, p. 484. 'Acad. des Sciences,' 1883, p. 1246. 'Archiv. de Physiologie,' 1883.
3. Baumgarten.—'Lehrbuch der Path. Mykol.,' Bd. ii, 1890. 'Monatschrift für prakt. Dermatol.,' Bd. iii, No. 7. 'Zeitschrift für wissensch. Microscopie,' Bd. i, 1884. 'Centralblatt für Bact. und Parasitenkunde,' Bd. i, p. 574.
4. Bonome.—'Virch. Arch.,' Bd. iii, p. 114.
5. Bordone Uffreduzzi.—'Zeitsch. für Hygiene,' Bd. iii, p. 178, 1887.
6. Cornil and Babes.—'Les Bacteries.'
7. Cornil and Suchard.—'Soc. Méd. des Hôpitaux,' June, 1881.
8. Damaschino.—'Arch. de Méd. expérimentale,' March, 1890.
9. Danielssen and Bock.—'Traité de la Spedalsked.' (Eng. translation).
10. Flügge.—'Micro-organisms,' p. 274, trans. by Watson Cheyne.
11. Hillis.—'Leprosy in British Guiana.'
12. Hutchinson.—'B. M. J.,' 1890, vol. i, p. 341.
13. Kaurin.—'Journal of Leprosy Committee,' vol. ii, 1891.
14. Kobner.—'Virch. Archiv,' 1882.
15. Koch.—'Berlin. klin. Wochenschrift,' 1882, p. 222. 'Micro-organisms and Disease,' New Sydenham Society.
16. Leloir.—'Mém. de la Société de Biologie,' 1885, p. 101. 'Traité théorique et pratique de la lèpre,' 1880.

17. *Lustgarten*.—‘Jahrbücher der K. K. Gesellsch. der Aerzte,’ 1885, p. 6.
18. *Lutz*.—‘Dermatolog. Studien,’ 1886, Heft 1. ‘Monat. für prakt. Dermat.,’ 1886.
19. *Neisser*.—‘Virch. Archiv,’ Bde. lxxxiv, xc, and ciii. ‘Verhandlung der Deutsch. Dermatol. Gesellschaft,’ Prague, 1889.
20. *Rake (Beaven)*.—‘Reports of Trinidad Leper Asylum.’
21. *Thin*.—‘Med.-Chir. Trans.,’ vol. lxvi, p. 314, 1883.
22. *Touton*.—‘Virch. Archiv,’ Bd. civ.
23. *Unna*.—“Leprastudien,” ‘Monat. für prakt. Derm.,’ 1884, 1885. ‘Dermatolog. Studien,’ 1886, Heft 1.
24. *Virchow*.—‘Onkologie,’ vol. ii.
25. *Voltolini*.—‘Breslauer Aertz. Zeitsch.,’ 1885, p. 173.
26. *Webb-Cook*.—‘Reports on Leprosy,’ Honolulu, 1886, Appendix P.
27. *Wesener*.—‘Centralblatt für Bact. u. Parasitenkunde,’ Bd. i, p. 450; Bd. ii.

